Sexually dimorphic effect of in vitro fertilization (IVF) on adult mouse fat and liver metabolomes.

Journal: Endocrinology

Publication Year: 2014

Authors: Sky K Feuer, Annemarie Donjacour, Rhodel K Simbulan, Wingka Lin, Xiaowei Liu, Emin Maltepe, Paolo F Rinaudo

PubMed link: 25211591

Funding Grants: SFSU Bridges to Stem Cell Research

Public Summary:
The preimplantation embryo is particularly vulnerable to environmental perturbation, such that nutritional and in vitro stresses restricted exclusively to this stage may alter growth and affect long-term metabolic health. This is particularly relevant to the over 5 million children conceived by in vitro fertilization (IVF). We previously reported that even optimized IVF conditions reprogram mouse postnatal growth, fat deposition, and glucose homeostasis in a sexually dimorphic fashion. To more clearly interrogate the metabolic changes associated with IVF in adulthood, we used nontargeted mass spectrometry to globally profile adult IVF- and in vivo-conceived liver and gonadal adipose tissues. There was a sex- and tissue-specific effect of IVF on adult metabolite signatures indicative of metabolic reprogramming and oxidative stress and reflective of the observed phenotypes. Additionally, we observed a striking effect of IVF on adult sexual dimorphism. Male-female differences in metabolite concentration were exaggerated in hepatic IVF tissue and significantly reduced in IVF adipose tissue, with the majority of changes affecting amino acid and lipid metabolites. We also observed female-specific changes in markers of oxidative stress and adipogenesis, including reduced glutathione, cysteine glutathione disulfide, ophthalmate, urate, and corticosterone. In summary, embryo manipulation and early developmental experiences can affect adult patterns of sexual dimorphism and metabolic physiology.

Scientific Abstract:
The preimplantation embryo is particularly vulnerable to environmental perturbation, such that nutritional and in vitro stresses restricted exclusively to this stage may alter growth and affect long-term metabolic health. This is particularly relevant to the over 5 million children conceived by in vitro fertilization (IVF). We previously reported that even optimized IVF conditions reprogram mouse postnatal growth, fat deposition, and glucose homeostasis in a sexually dimorphic fashion. To more clearly interrogate the metabolic changes associated with IVF in adulthood, we used nontargeted mass spectrometry to globally profile adult IVF- and in vivo-conceived liver and gonadal adipose tissues. There was a sex- and tissue-specific effect of IVF on adult metabolite signatures indicative of metabolic reprogramming and oxidative stress and reflective of the observed phenotypes. Additionally, we observed a striking effect of IVF on adult sexual dimorphism. Male-female differences in metabolite concentration were exaggerated in hepatic IVF tissue and significantly reduced in IVF adipose tissue, with the majority of changes affecting amino acid and lipid metabolites. We also observed female-specific changes in markers of oxidative stress and adipogenesis, including reduced glutathione, cysteine glutathione disulfide, ophthalmate, urate, and corticosterone. In summary, embryo manipulation and early developmental experiences can affect adult patterns of sexual dimorphism and metabolic physiology.